Neuro-Pharmacological screening of plant constituents extracted from Mucuna Puriens and Boswella Serrata: Potential for Huntington's disease Treatment

Synopsis

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Table of content

1. Introduction……3

2. Scope of work……6

3. Rationale……7

4. Review of Literature……..9

5. Aim…..14

6. Objective…….14

7. Plan of work……15

8. Materials and methods…..16

9. Probable out come….16

10. References….18

1. Introduction:

Neurodegenerative diseases are growing very fastly across the globe and showing a burden on the society (Ayoobi et al., 2017). The World Health Organization (WHO) estimates that more than one billion people suffer from central and peripheral nervous system (CNS/PNS) disorders globally (Duraes et al., 2011). These diseases include Parkinson's disease, Huntington disorder, epilepsy, schizophrenia, bipolar disorder, Alzheimer's disease and other dementias, neuroinfections, multiple sclerosis, brain tumors, traumatic disorders, and cerebrovascular diseases such as stroke and migraine.

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder resulting in a neuronal degeneration in the striatum, followed by degeneration of the cerebral cortex and striatum during later stages of the disease. The basis of huntingtons disease is a CAG repeat expansion >35 CAG in a gene that codes for ubiquitous protein known as 'huntingtin'. This results in abnormally long polyglutamine tract in the protein N-terminus that leads to protein aggregation in brain causing neuronal loss. (Anton Reiner et. al., 2011) The initial clinical manifestations include personality and mood changes which are sometimes followed by a cognitive decline, andthen involuntary choreiform movements, bradykinesia, dystonia (in some patients), rigidity, and dementia ultimately leading to death approximately 15–20 years from the age at onset (Ross, and Tabrizi, 2011)

Anumber of common pathophysiological features have been proposed for these diseases, including elevated oxidative/nitrosative stress, mitochondrialdysfunction,protein misfolding/aggregation, synapse loss, and decreased neuronal survival (Finkel et al., 2011). More than 6 million people reportedly die each year due to neurological disorders, with over 80% of these deaths occurring in low- and middleincome countries. Neurological problems are the second largest cause of mortality and first largest cause of disability worldwide.

Moreover, although little research attention has been paid to neurological disorders(Winner et al., 2011) In addition, the CNS disease burden is exacerbated by the numerous but understudied neurological impairments associated with common tropical diseases such as the neglected tropical

diseases (Shirooie et al., 2018). For several neurological disorders, modern medicine offers symptomatic treatment that is often expensive and associated with side effects. Indian system of medicine has traditionally been used in several neurological conditions. The accessibility, cost effectiveness and lower incidence of side effects of plant products offer considerable advantages. Various laboratories have been involved in investigating the efficacy and mechanism of action of Indian medicinal plants in experimental models of stroke, Alzheimer and epilepsy.

Medicinal plants are used for hundreds of years as remedies for human diseases and animals. Intensive studies on adverse effects of herbal medicines are being done and the institution of a decent correlation between biomarkers and plants square measure essential for guaranteeing the potency and quality of herbal medicines. In previous few decades, there has been growing interest in exploiting biological activities of plant-based medicines because of their natural origin, cost effectiveness and lesser facet effects. Medicinal plants are used by almost 80% of the world's population for their basic health care because of their low cost and ease in availability (Shazadi et al., 2010). From the dawn of civilization, people have developed a great interest in plant-based drugs and pharmaceutical products and their use in disease management (Shazadi et al., 2010).

Studies evaluated herbal extracts and natural products (*Withanolides,* alpha-tocopherol, melatonin and vineatrol, diosmin, Biocanin, Morin hydrate, Papavarine) in the various neurological problems. The study based on magnetic resonance imaging, assessment of neurological deficit, battery of motor performance tests and markers of inflammation, Mitochondrial studies and oxidative stress revealed the therapeutic potential of these plant products. Moreover, various plant extracts were also evaluated for their potential antiepileptic activity in various experimental models of epilepsy in rats. Herbal extracts and natural products including *Acorus calamus*, *Anacyclus pyrethrum, Benincasa hispida, Orchis mascula, Centella asiatica, Zizyphus jujuba* and curcumin showed antiepileptic effect. These agents can be used as an adjunts to antiepileptics, antiparkinsonism and memory enhancer for increasing their efficacy and decreasing the side effects, particularly cognitive impairment.

Phytochemistry is concerned with the enormous variety of substances that synthesized and accumulated by plants and deals with structural elucidation of these substances. The technology involving the extraction, purification and characterization of pharmaceuticals from natural sources

is the significant contribution to the advancements of natural and physical science. Plant-based natural constituents can be derived from any a part of the plant like bark, leaves, flowers, roots, fruits, seeds, etc. Helpful properties of plants distinctive to explicit plant species are analyzed or teams square measure in step with the conception that combination of secondary product during an explicit plant is taxonomically distinct.

The use of herbal medicinal plants has always played a positive role in the control or prevention of diseases such as neurological disorder, metabolic disorders and various other problems. Medicinal plants are now getting more attention than ever because they have potential of myriad benefits to society or indeed to all mankind especially in the line of medicine and pharmacology. The medicinal value of these plants lies in bioactive phytochemical constituents that produce definite physiological action in human body (Akinmoladun, 2007). The WHO has estimated that for some 3.4 billion people in the developing world, plants represent the primary source of medicines. This means that 88% of the world's population mainly relies on traditional herbal medicines for their primary health care (Farnsworth, 1988).

Nearly 50% all drugs sold in the developed world have their origins from natural sources. Nine out of top 20 swelling drugs were derived from natural sources and generated more $16 billion (US) in 1998 up to 80% of all anticancer and antibacterial drugs have come from natural sources. For example, drugs that are derived from nature include: anti-infectives, anti-cancer agents (taxol), CNS drugs (cannabis), cardiovascular drug (Digixon), analgesics (opioids, aspirin) and cholesterol lowering drugs (Pravastatin) and neuroprotective drugs (Gingco biloba). Pacitaxal, derived from Taxus brevefolia, is the drug of choice in several cancers including breast cancer. Vinblastin and vincristine are Chemicals discovered in Vinca in 1950s.Vinblastin is the first choice of drug of choice in many forms of Leukemia and Since the 1950s it has increased the survival rate of childhood leukemias by 80% (Ali, 2015). In India there are innumerable medicinal plants whose active constituents have not yet been explored by researchers.

2. Scope of work:

The mechanisms underlying the pathogenesis of neurological disorders are not well understood. Attempts to improve the efficacy of neurological drugs have focused on reducing the latency of the response and on finding strategies for treatment-resistant cases. This has created expectations that greater efficacy in subgroups could be achieved with new molecules and different mechanisms of action and newer treatment strategies are, therefore, directed at pharmacological targets. Despite initial promise, the development of herbal medicines to treat neurological disorders has been not advanced significantly. This is due to an incomplete understanding of the phytoconstituents and molecular mechanism of active constituents.

It is estimated that about 50% of patients with neurological problems fail to adequately respond to a first line therapy, and more than 30% of these patients are resistant to a series of treatments. Clinically, this is referred to as one of the most challenging aspects to the successful management of neurological problems.The delayed onset of action with the available drugs poses several challenges in the treatment of neurodegenartive disorders. Further, the high co-morbidity can lead to changes in diagnosis during the course of the illness, further confounding the discovery of novel drugs. Attempts to improve the efficacy of neurological disorders treatments have focused on reducing the latency of the response and on finding strategies for treatment-resistant cases and to explore the molecular mechanism. Moreover, despite increased interest among the clinical neurosciences, there are still rooms to explore the neurological potentials of Boswellia Serrata and Mucuna Puriens for clinical use in neurology. It is therefore necessary to screen these plant extracts and active constituents for their potential in CNS disorders.

Barriers in Current therapy

- Efficacy and Adverse Effect (AE) profile
    - Existing drugs similarly effective - extensive but varied AE profile
- Treatment resistant patients
    - 20% patients do not respond to current therapy
- Onset of action
    - Existing drugs take weeks to show significant benefit
- High co-morbidity
    - Treatment of both problems will be advantageous

- Novel treatments are required
    - Difficult to develop without understanding mechanism

Scope of the work will be to overcome the a fore mentioned limitations on Huntington's disease therapy

- Fast onset
- Improved and broader efficacy (co-morbidity)
- Fewer Adverse effects

To address these needs, there are numerous plant medicines that have been identified that may demonstrate improvements in one or more areas such as antioxidant, based on recent findings that antioxidant property of herbal medicine can help to improve neurological symptoms

3. Hypothesis/Rationale:

Neurological disorders are complex, heterogeneous disorders and several neurotransmitter and neurohormonal pathways have been implicated in the pathophysiology. The pathology of the Huntington disease has been attributed to toxic gain of functions for the mutant Huntington protein, such as protein aggregation, transcriptional dysregulation, defective energy metabolism, oxidative stress, excitotoxicity, and inflammation (Kumar et al., 2014), as well as to the loss of beneficial functions of wild type Huntington protein (Htt), which includes BDNF translation, vesicle transport and as scaffold for autophagic machinery (Ochaba et al., 2014).A number of laboratories have provided evidence supporting the hypothesis that oxidative stress is a primary event in HD neuropathology (Sorolla et al., 2008). Nevertheless, trials involving classical "antioxidants" in human HD patients have largely been unsuccessful.

Mucuna pruriens variant utilis (MP) is a leguminous plant growing spontaneously in tropical/subtropical areas worldwide, whose seeds contain high concentrations of levodopa 6. MP-based therapy may become a potential alternative to marketed levodopa-based medications, because it is easy to find at local markets and requires a low-cost preparation method with- out pharmacologic processing. Preclinical and clinical studies suggest that MP powder extract may be

used to improve neurological disorders with a favorable safety profile (Manyam et al., 2004; Saranya et al., 2020). Thus based on other studies and potential of both the plant to treat a lot of disorder due to potential anti-oxidant activity may be use for the treatment of neurological disorders (Ameh et al., 2020).

Extracts from oleo gumresin of Boswellia serrata, in India called salai guggal, have been described in Ayurvedic text books (Charaka Samhita, 1st–2nd century AD and Astangahrdaya Samhita 7th century AD) as a remedy for the treatment of a variety of inflammatory diseases and CNS disorders. Boswellia serrata is a tree of the Burseraceae (frankincense) species that abundantly grows in India, Africa and the Middle East. The oleo gum resin of Boswellia serrata has been traditionally used in folk medicine for a variety of therapeutic purposes such as headache, hyperlipidemia, colitis (Gupta et al., 2001), arthritis (Sharma et al., 1989), cancer and inflammation (Singh and Atal, 1986).

Mucuna pruriens and Boswellia serrata extract was shown to modulate oxidative stress status (lipid peroxidation, GSH, catalase, superoxide dismutase, and nitrite oxide levels) in arthritis (Umar et al., 2014). Moreover, the antioxidant and free radical scavenging activity of B. serrata extract was reported by several in vitro studies (Singh et al., 2012; Beghelli et al., 2017). Thus, the neuroprotective effect of mucuna pruriens and Boswellia serrata extract could behelpful in treating huntigton disorders.

4. Review of literature

It is important to emphasize that while molecular events, such as transcriptional dys-regulation, protein aggregation, and mitochondrial dysfunction, have been linked to HD pathogenesis, it is still not clear whether oxidative stress causes HD, or is a consequence of more primary events (Achour et al., 2015). This uncertainty provides a compelling reason to review the

putative molecular regulatory connections between redox changes and the established early events, such as mHtt aggregate formation and transcriptional dysregulation. Additionally, we will critically analyze the current support for a role for oxidative stress in HD, the shortcomings that have hindered progress and alternative redox therapeutic options that should dominate attention of the field to potentially achieve better therapeutic success in Huntington's disease.

Oxidative stress can be operationally defined as an imbalance between oxidants and antioxidants, in favor of oxidants, sufficient to result in cell damage, dysfunction or death. Oxidants are short-lived molecules with an unpaired electron in one or more of their outer orbitals and, therefore, they have the theoretical capacity to steal electrons from any cellular constituent, including proteins, lipids, and DNA. Cells produce these oxidants either in the form of reactive oxygen species (ROS), reactive nitrogen species (RNS), or reactive lipid species (RLS).

Huntington's diseaseand Aberrant Redox Signaling

Currently, ROS are well established as signaling molecules involved in a variety of signal transduction pathways, but very few of these signaling pathways have been examined in the context of oxidants and HD. Rather, most of the information regarding the redox regulation of signaling is currently emerging from the cancer field. For instance, cell survival pathway, such as the Erk pathway, is regulated in a redox associated manner by mitogen activated protein kinase phosphatase-3 (MKP-3). MKP-3 has a reactive cysteine whose oxidation results in inactivation of the phosphatase activity, leading to activation of the ERK pathway (Seth and Rudolph, 2006). Besides this, cas-pases contain a reactive cysteine, which regulates their activity. Under physiological conditions, mitochondrial caspase 3 and 9 are nitrosylated and, therefore, inactive while in the presence of pro-apoptotic signals, caspases get activated through the denitrosylation of their reactive cysteines (Mannick et al., 2001). Likewise, the activity of chaperones involved in proper protein folding, such as Hsp70, Hsp90 and PDI, are also redox-regulated through the reactive cysteine residues present in these proteins (Tsai et al., 2001)

Roberto Cilia et al., 2014

This study aims to investigate whether the efficacy of MP powder is no inferior to levodopa/benserazide, the intake of MP powder at suprathreshold dose is safe, and the effects

ofMP are similar to those of a pharmaceutical preparation of levodopa alone. This study demonstrates that the acute intake ofMP powder at both high and low dose is no inferior to dispersible levodopa/benserazide in terms of all efficacy and safety outcome measures. Both low-dose and high-doseMP were superior to placebo. Low-dose MP was associated with a motor response that was equivalent to the response to evodopa/benserazide, while high-dose MP induced a qualitatively better motor response than LD1DDCI along with longer duration of the on state by about 45 minutes and fewer dyskinesias.

Roberto Cilia et al., 2017

This is an open-label, no inferiority, randomized, crossover, phase-2b pilot trial consisting of two 8-week treatment phases, plus two dose-adjustment periods before each treatment phase. Eighteen patients were assessed for eligibility and 14 were randomized to MP or LD/CD. The purpose of this study was to prove the no inferiority of MP powder compared to LD/CD over a 16-week period in terms of efficacy and safety. The primary efficacy outcome measure was the difference in mean change at 8 weeks in quality of life between the two treatments, as assessed by the use of the summary index of the 39-item . Safety was evaluated by parameters including (i) frequency of adverse events (AEs) and AEs leading to treatment discontinuation, (ii) clinical laboratory tests (including all functions potentially influenced by MP according to the literature, (iii) electrocardiography.

Daily intake of Mucuna pruriens as the only source of levodopa in patients with advanced PD was comparable to marketed LD/CD in primary and secondary efficacy measures. However, 50% of patients discontinued prematurely due a combination of gastrointestinal complaints and/or progressive shortening of the ON time as for the development of drug tachyphylaxis (after a relatively short-term exposure). All the issues arisen in this pilot study have greatly improved our understanding of the management of MP-based therapy in PD and can be considered as a roadmap guide to planning future trials on larger populations.

Ammon, 2010

Anti-inflammatory activity of an extract of the gum resin of Boswellia serrata in animal experimentsis reported earlier. Extracts from the gum resin of Boswellia serrata and other

Boswellia species aswell as some of its constituents including boswellic acids and others have been shown to affect parameters of the immune system in different ways. As far as the humoral defence system is concerned boswellic extracts and boswellic acids affect antibody titres and immunglobines. Here, it appears that in mice oral doses of 50mg/kg and less are stimulatory whereas higher doses tend to show the opposite. The same holds for the proliferation of lymphocytes. A further target of BEs and BAs in the immune system is the complement system where inhibiton of C3-convertase was reported.

Sharma et al., 1996

This study deals with the effects of Boswellia extracts, Boswellic acid and other constituents of on NFK-beta and cytokines. The activation of the transcription factor was shown to be inhibited by AKBA and probably also of other compounds including incensole acetate and 12-ursene-2-diketone suggesting decreased transcription of factors related to inflammation including a variety of cytokines. Among the factors are proinflamatory interleukines TNF- IL-1, IL-2, INF-, IL-6, IL-12, but also upregulation (IL-4, IL-10) was observed.

Sharma et al., 1996

Humoral antibody synthesis was tested by in the serum from mice treated with sheep erythrocytes by determining the hemagglutinating antibody titres. It was found that a single oral dose of a mixture of BAs (50–200mg/kg) on the day of sensitisation produced a dose related reduction (10.4–32.8%) in primary hemagglutinating antibody titres on day 4. A significant reduction in antibody production was obtained with 100 and 200mg/kg doses. On the other hand the secondary antibody titres were significantly enhanced at lower doses, the effect being more prominent at 50mg/kg. Azathioprine as a reference compound (200mg/kg p.o.) administered following the same schedule resulted in only 10.4% inhibition of primary antibody synthesis and had no effect on the secondary antibody production. Using the technique of complement fixing, a method for analyzing antigen and antibody titres, oral administration of amixture containing BAs (25, 50, 100mg/kg) for 5 days around the time of immunization resulted in a significant decrease in primary and sec ondary complement fixing antibody titres at 100mg/kg.

Khajuria et al., 2008

Previously it was shown that oral administration of a biopolymeric fraction (BOS 2000) from Boswellia serrata (1–10mg/kg) elicted a dose related increase in the delayed hypersensitivity reaction (early 24h and delayed 48h) inmice. It also stimulated the IgM and IgG titre expressed in the form of plaques (PFC) and complement fixing antibody titre. From these studies where either a mixture of different boswellic acids or a biopolymeric extract of BS has been employed, it appears that lower doses exhibit a humoral immunstimulating action, whereas this effect is attenuated or even reversed with increasing the dose.

Gayathri et al., 2007

Two studies investigated the effect of an extract of Boswellia carterii Birdw and of BAs in the lymphocyte proliferation assay. This in vitro test utilizes sensibilized lymphocytes, especially T- lymphocytes and is used to establish immunomodulatory activity. It is reported that, if spleen cells from non immunizedmicewere used, amixture of various BAs in the range of 1.95–125.0g/ml showed no spontaneous mitogenic activity and the cell viability was comparable to controls. When the test was performed in the presence of mitogen stimulating lipopolysaccharides (LPS),phytohaemagglutinin(PHA), concanavalinA(ConA) and alloantigen, a concentration dependent inhibition of lymphocyte proliferation was observed.

From study, it appears possible that the antiinflammatory action of BAs or other constituents of BEs starts with the inhibition of NFK-beta-B activation observed that a crude methanolic extract m BS and 12-ursine-2-diketone, a pure compound of BS, inhibited TNF-alpha, IL-1 and IL-6 in cultured PBMCs. Observations on Th1/Th2 cytokines revealed marked down gulation of IFN-and IL-12 whereas IL-4 and IL-10 were regulated upon treatment with a crude extract and the pure mpound 12-ursene-2-diketone indicating that both are capable carrying out anti-inflammatory activity at sites where chronic flammation is present by switching off the proinflammatory cytokines.

Clinical studies

There are variety of clinical studies dealing with the effects of BEs in chronic inflammatory diseases including rheumatoid arthritis (Etzel 1996), bronchial asthma, ulcerative colitis (Gupta et al. 1997), Crohn’s disease, Osteoarthritis (Kimmatkar et al. 2003; Sengupta et al. 2008; Sontakke

et al. 2007) suggesting improvement. It is possible that this is due to different actions of BEs/BAs on factors/mediators of the immune system.

Hamid Reza Sadeghnia,2017

The present work aimed to test whether Boswellia serrata hydroalcoholic extract (BSE) and AKBA may protect neuronal cells against oxygen, glucose and serum deprivation (OGSD)-induced cytotoxicity, an in vitro model which simulates neuronal damage during ischemia.The neuroprotective effect of Boswellia serrata observed in this study is in concert with reports from Jalili et al. that aqueous extract of this plant increase the number of neuronal processes in the hippocam pus and improves learning deficit in both normal and kindled rats. An in vitro study also showed that β-boswellic acid could increase neurite out growth and branching of primary cells of hippocam pal tissue in rats. In patients suffering from cerebral edema due to brain tumors, administration of Boswellia serrata significantly reduced the volume of edema. This effect may be mediated in part by anti-inflammatory action of Boswellia serrata.

This study was performed to examine the protective effects of BSE against neuronal injury induced by OGSD, which mimic the pathological features of cerebral ischemia. Since the pharmacological effects of Boswellia serrata are mainly attributed to the pentacyclic triterpenoid boswellic acids, especially AKBA, the possible neuroprotective effect of this compoundwas also examined. Our results demonstrated that incubation with BSE and AKBA can inhibit cell death under OGSD condition. The neuroprotective effect of BSE and AKBA was more obvious at concentration of 2.5 µg/mL and 1 µg/mL, respectively. Our data showed that BSE and AKBA were able to prevent the increase of intracellular ROS and the enhanced lipid peroxidation in OGSD condition.

Forouzanfar et al., 2016

Recently, numerous publications reported the encouraging results of Boswellia serrata on a variety of inflammatory disorders, such as asthma, inflammatory bowel disease, osteoarthritis and rheumatoid arthritis. Moreover, it reduced peritumoral brain oedema accompanying glioma. Also, it has been shown that Boswellia serrata resin possesses strong antioxidant and immunomodulatory properties. Based on the antioxidant and antiinflammatory effects of

Boswellia serrata, the current study was carried out to estimate the effects of Boswellia serrata extract on ischemic cerebral injury induced by middle cerebral artery occlu sion (MCAO) in rats. Our results revealed the neuroprotective potentials of Boswellia serrata extracts and the biologically active constitu ent, AKBA, against focal cerebral ischemia in rats in a dose-dependent manner, which were confirmed by im provement in neurological deficits, reduced cerebral infarction, neuronal cells loss and apoptosis, and also improved cerebral redox status.

5. Aim:

The present study is designed:

To perform the phytochemical analysis of chemical constituents extracted from Mucuna Puriens and Boswella Serrata for neuro-Pharmacological activity.

To evaluate the potential of extracted plant constituents for the treatment of Huntigton's disorder.

6. Objectives

- To prepare different extracts and fractions of plants from the solvents of varying polarities.
- To carry out preliminary phytochemical analysis of crude extracts and various fractions prepared for the detection of the type of phytoconstituents present.
- To carry out isolation and purification of phytoconstituents present.
- To study the acute toxicity for determination of LD50 of the extract's fractions/phytoconstituents
- To perform the *in-vitro* antioxidant study of plant extracts fractions/phytoconstituents to evaluate potential antioxidant activity in different assay
- To perform the beneficial effects of individual plant extracts fractions/phytoconstituents in 3NP-induced huntigton's disease.
- To prepare formulation of plant extract and evaluate the neuro-pharmacological activity on huntigton's disease

7. Plan of work:

Phase 1. Literature Survey

Literature Review. A thorough literature survey will be pursued for selection of plant and tests to constitute the complete neuro-pharmacological screening process.

Phase: 2

Collection and authentication of plant material

Phase: 3

Morphological study

Preparation of extracts

Preliminary phytochemical studies

Standardization of extract and Isolation of active chemical constituents

Phase: 4

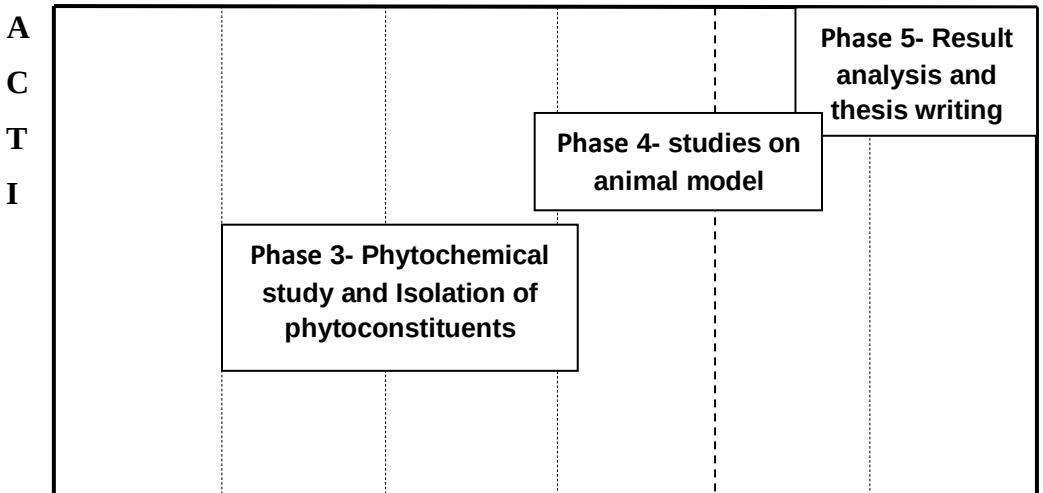
In-vivo studies to identify the neurological potential of plant extracts/active constituents in 3NP-induced neurological disorders. The biochemical parameters will be also evaluated

Phase: 5

Assessment

Analysis of the pre-clinical data, drawing of conclusions based on results obtained and thesis writing.

<u>WORK PLAN</u>: TENTATIVE DURATION OF WORK



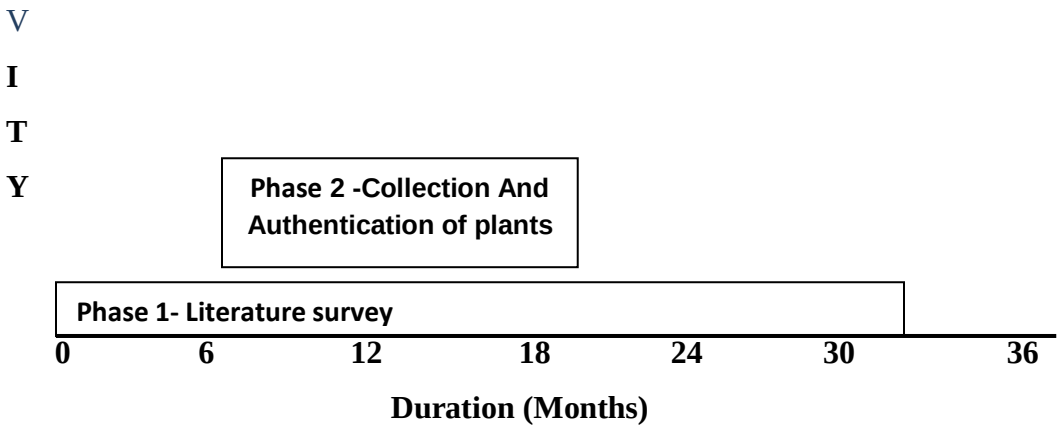


Figure 1: Tentative schedule to perform different activities

8. Materials and methods

Plant Material

Collection and Authentication of Plant

Fresh parts of plants will be collected, taxonomically identified and authenticated from botanist.

Standardization parameters of plant extracts

Estimation of Foreign organic matter

Estimation of Ash values

Estimation of loss on drying of plant extracts

Extractive values of different extracts of plants

Determination of water soluble extractive value

Determination of ethanol soluble extractive value

Determination of chloroform soluble extractive value

Preparation of the leaf and bark part extracts of Plants

The extraction of leaf and bark parts of both plants in different solvents will be performed as per the following

Preliminary phytochemical screening of plant extracts

All the extracts of plants will be subjected to preliminary phytochemical investigation for the detection of the following metabolites: (1) alkaloids, (2) carbohydrates, (3) glycosides, (4) phenolic compounds, (5) flavonoids, (6) protein and free amino acids, (7) saponins (8) sterols (9) acidic compound, (10) steroids, (11) fixed oil and fats and (12) terpenoids

Quantitative estimation of extracts of plants

Estimation of total phenolic content

Estimation of tannin content

Determination of total flavonoid content

Standardization of extracts

Quantitative analysis

TLC analysis of extracts of plants

HPTLC fingerprint Development

Isolation and Characterization of Phytoconstituents of Plants by Column Chromatography

Spectral analysis of Plants extract

UV spectra of the samples

IR spectra of the samples

Nuclear magnetic resonance spectroscopy

***In-Vitro* antioxidant assay:**

***In-vivo* testing**

Acute toxicity study

Assessment of potential of plant extracts in 3-NP induced neurological problem

Blood samples for biochemical estimation:

9. **<u>The Relevance and Expected outcome of the proposed study</u>**

The major problem with the resistant and delay in onset of action is the tremendous suffering in neurodegenerative diseases. People may be bedridden; they may have disruption in their personal, professional lives, literally unable to function adequately, which really disrupts the

life of an individual ultimately leading to death of the patient after several years. Till date there is no any complete curative therapy for neurodegenerative diseases. So, if drugs with potential to treat neurological disorders will produce fast action with lower side effects, it would be great in minimizing the disturbance in the personal, professional life of that individual.

From the pharmacological point of view, the development of new molecules from plant sources appears to be a sensible approach to pursue the outstanding clinical needs in CNS disorders. By employing advanced animal model of neurodegeneration, like 3-NP induced huntigton's disorders and molecular estimation of various enzymes made feasible to probe potential of plant medicine in the treatment of neurodegenerative diseases.

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